

REMARKS

Reconsideration of this application is requested.

Claims 1-17, with amendments discussed below, remain pending for consideration.

With reference to the Examiner's comments in the first ¶, page 2 of the action, an IDS with PTO-1449 citing the references noted in the specification and in the International Search Report is being submitted herewith. The Examiner is requested to consider the cited references in the examination of this application.

Claims 4 and 11 have been amended in response to the Examiner's Section 112 rejection of these claims. The changes in the claims and the manner in which they deal with the Examiner's objections are thought to be self-evident. Thus, claim 11 has been amended to provide antecedent basis for the reference back to claim 6. Additionally, the "calculated as aglucon" has been deleted as unnecessary from claim 4. The claims, as amended, are thought to be clear and definite and otherwise acceptable as to form.

The Examiner is respectfully requested to reconsider the Section 103(a) rejection of the claims as unpatentable over Green et al. (U.S. 2002/0068121) in view of Kuhrts (U.S. 2003/0091656). The references do not make the applicant's invention obvious.

In rejecting the claims, the Examiner notes that Green et al. discloses a blend of quercetin and either one of genistein, diadzein or glycitein isoflavones. The Examiner further notes that Green et al. fail to disclose hops isoalpha acid. However, the Examiner takes the position that it would be obvious to substitute a hops isoalpha acid, as used in Kuhrts, for the Green et al. quercetin, for the purpose of obtaining an anti-inflammatory effect.

The applicant submits that the Examiner's rejection should be withdrawn as there are several important reasons why the references cannot make the applicant's invention obvious.

For one thing, Green et al. is only concerned with blends of different isoflavones. There is no motivation for the skilled person to substitute a completely different chemical entity for one of the Green et al. isoflavones. All of the isoflavones referred to in Green et al. have very similar chemical structures, including quercetin itself which the Examiner believes could be replaced by a hops iso-alpha acid in an obvious manner. With respect, however, it is submitted that hops isoalpha acids are structurally very different from isoflavones, including quercetin.

Attached hereto is a sheet showing the chemical structure of quercetin, genistein and diadzein. A second sheet attached shows the chemical structure of humulone. Humulone is a typical hops iso-alpha acid and all the preferred iso-alpha acids recited in the instant application are humulone or a humulone derivative. The Examiner will appreciate from the attachments that

the structure of humulone is very different from the structure of quercetin, genistein and diadzein. Thus, there is no reason at all why the skilled person would think of replacing quercetin in a blend of structurally very similar isoflavones disclosed in Green et al. with a structurally very dissimilar hops iso-alpha acid from Kurhts. Clearly, there is nothing in either reference to suggest the modification needed in Green et al. to reach the applicant's invention.

Furthermore, although Green et al is concerned with inhibition of inflammation in the skin, Kuhrts is only concerned with arthritic inflammation. This is another significant reason why the skilled person would not think to combine the teaching of the two references. After all, the respective purposes of the references are substantively different.

Finally, the applicant notes that Example 2 of the present application provides incontrovertible proof that the claimed hops iso-alpha acids and isoflavones act synergistically in combination to combat skin inflammation, more especially inflammatory conditions in the skin associated with ageing. There is nothing in the references suggestive of this result.

Thus, in summary, the applicant's invention is not obvious from the Examiner's references because there is a total lack of motivation to combine the references to reach the invention and there is an unpredictable and unexpected synergistic result from the claimed combination.

In the circumstances, the applicant submits that the Examiner's Section 103(a) rejection should be withdrawn with allowance of all of the claims herein.

Favorable action, consistent with the above, is requested.

Respectfully submitted,

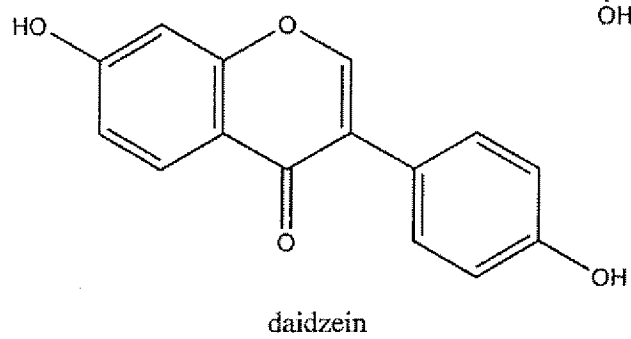
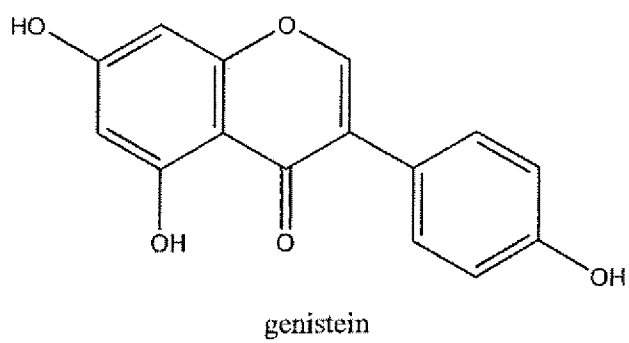
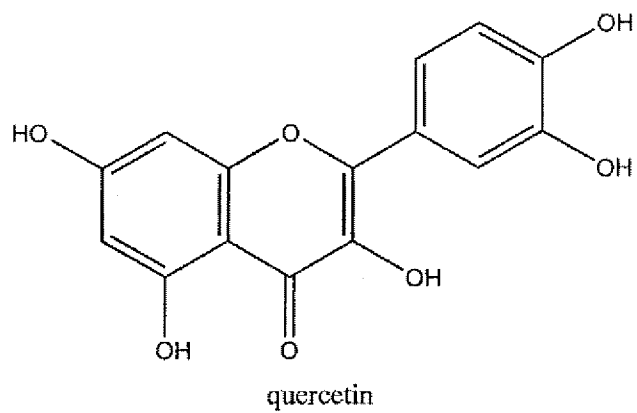
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Date: March 17, 2009

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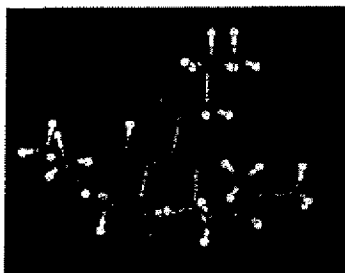


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HUMULONE



Humulone 3D Molecular Structure

Hops

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Skip Hop Bags - SALE

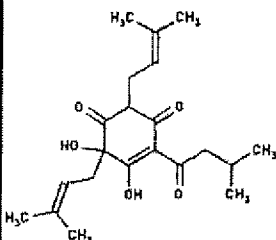
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Humulone is one of the bitters in the hop. The hop (*Humulus*) is a small genus of flowering plants, native to the temperate Northern Hemisphere. The female flowers, commonly called hops, are used as flavouring and stabilizers during beer brewing.

Humulone has a chemical formula of: $C_{21}H_{30}O_5$



Hop resins are composed of two main acids: alpha and beta acids. Alpha acids have a mild antibiotic/bacteriostatic effect against Gram-positive bacteria, and favours the exclusive activity of brewing yeast in the fermentation of beer. The flavour imparted by hops varies greatly by variety and use: hops boiled with the beer (known as "bittering hops") produce bitterness, while hops added to beer later impart some degree of "hop flavour" (if during the final 10 minutes of boil) or "hop aroma" (if during the final 3 minutes, or less, of boil) and a lesser degree of bitterness. Adding hops after the boil, a process known as "dry hopping", adds hop aroma, but very little bitterness. The degree of bitterness imparted by hops depends on the degree to which otherwise insoluble alpha acids (AAs) are isomerised during the boil, and the impact of a given amount of hops is specified in International Bitterness Units. Unboiled hops are only mildly bitter. Beta acids do not isomerise during the boil of wort, and have a negligible effect on beer flavour. Instead they contribute to beer's bitter aroma, and high beta acid hop varieties are often added at the end of the wort boil for aroma. Beta acids oxidise and oxidised beta acids form sulphur compounds such as DMS (dimethyl-sulfide) that can give beer off-flavours of rotten vegetables or cooked corn.

"Noble hops" are low in bitterness and high in aroma, and traditionally consist of four central European cultivars, 'Hallertauer Mittelfrüh', 'Tettnanger', 'Spalter', and 'Saaz'. They contain high amounts of the hop oil humulene and low amounts of alpha acids cohumulone and adhumulone, as well as lower amounts of the harsher-tasting beta acids lupulone, colupulone, and adlupulone. Humulene imparts an elegant, refined taste and aroma to beers containing it. These hops are used in pale lagers.

The medically active ingredients in Hops are humulone and lupulone.

Humulene, or α -humulene or α -caryophyllene, is a naturally occurring monocyclic sesquiterpene. It is found in the essential oils of *Humulus lupulus* (hops) from which it derives its name, *Lindera strychnifolia* and others. It is an

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